Myeloid Leukemia in the Rabbit (Oryctolagus cuniculus)

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SUMMARY

We report the first case of myeloid leukemia in the rabbit; it occurred in a 13.5-month-old strain III\textsubscript{ep} male. Its features are distinct from hereditary lymphomas and accessory sex organs (3). Ideally, for oncogenic studies, tumors occurring with high frequency in rabbits of 1 year of age or less are required. We have described such a situation in the partially inbred strain WH, in which we have found 63 cases within a few years; susceptibility is conferred by a single autosomal recessive gene, \textit{ls}. Affected rabbits die at around 8 months of age (4). A hereditary, immune-hemolytic anemia occurs in the genetically related incipient inbred strain X; to date, we have observed 57 cases. This disorder is usually fatal at 4 to 5 months of age; however, in a few protracted cases, thymomas developed. A single, autosomal, recessive gene, \textit{ha}, confers susceptibility (5). The association of thymoma and lymphoid hyperplasia with hemolytic anemia is of considerable interest because of its analogy to similar situations in man and NZB mice.

Prior to our reports of lymphosarcomatosis, probably fewer than 30 cases of neoplasms of the hematopoietic system have been described in the rabbit (16). Myeloid leukemia has never been reported in rabbits. Because of its apparent rarity, we are describing the first such case in the rabbit.

CASE REPORT

The afflicted male rabbit of strain III\textsubscript{ep} died at 13.5 months of age. Following necropsy, tissues were fixed in 10% buffered formalin, embedded in paraffin, sectioned at 10 \mu m, and stained with hematoxylin and eosin, Gomori's iron stain, Giemsa, and Gridley's reticulum stain.

Strain III\textsubscript{ep} is a partially inbred subline of strain III, selected for susceptibility to sound-induced epileptiform seizures (for strain characteristics, see Refs. 2, 6, 8, 9, and 10). The affected rabbit, \delta 693406, was seizure prone and, thus, of the genotype ep/ep. Standard genetic tests are being instituted to determine whether this case of myeloid leukemia may have a hereditary basis.

Two gross features were outstanding in this rabbit: a greatly enlarged and blood-engorged spleen and a visibly absent thymus. Although the major mesenteric lymph node was moderately enlarged, no other lymphadenopathy was observed. The liver was mottled, the adrenals were enlarged, and the blood was "watery-thin" from apparent anemia. Histologically, there was a generalized lymphoid atrophy. Lymph follicles, including the Malpighian corpuscles of the spleen, were extremely small. In contrast, the lymphoid sinuses and splenic red pulp were filled with lymphocytes and fibrous tissue. These were pleomorphic and usually contained small, irregular, and segmented nuclei and large amounts of pale cytoplasm. Many were neutrophils containing pseudoeosinophilic granules. They invaded the capsules and trabeculae of spleen and lymph nodes, thus further obliterating their normal architecture. Sinuses and blood vessels were entirely packed with tumor cells, suggesting a highly elevated WBC count. In fact, the spleen contained numerous small infarcts consisting of necrotic tissues and large amounts of iron-positive deposits.

Clusters of small, dense, nucleated cells occurring throughout the viscera represented foci of extramedullary hematopoiesis. All viscera were infiltrated to varying degrees by undifferentiated polygonal and reticular cells. These infiltrates were particularly prominent in and around the portal triads. These perportal aggregations produced a considerable amount of reticulum, but fibrosis occurred in the spleen as well. Pertinent microscopic features are depicted in Fig. 1, \textit{a} to \textit{d}.

DISCUSSION

The leukemic cell types in this rabbit are clearly of myeloid origin. They are reticular stem cells that are reticulin-producing to readily identifiable segmented myeloid cells, including neutrophils or so-called pseudoeosinophilic granulocytes.

The neoplastic cells are different from the lymphoblasts occurring in the hereditary lymphosarcoma of strain WH. Lymphosarcoma is characterized by uniformly large lymph nodes that are cream colored, by prominent Peyer's patches,
by splenomegaly, and often by a grossly enlarged thymus. The most conspicuous gross lesion in the present rabbit was a severe splenomegaly with neither thymic enlargement nor generalized lymphadenopathy. Furthermore, and in contradistinction to lymphosarcomatosis, the WBC count easily must have been 100,000/cu mm or higher, whereas the WBC count in lymphosarcoma is usually in the normal range from 6,000 to 10,000/cu mm.

We have tentative evidence that ha and Is are alleles, the different phenotypic expressions being caused by the differences in the remainder of the genotype of strains WH and X. In the light of these genetic considerations in rabbits and by analogy to the known strain and age dependence of myeloid leukemia in Mus musculus, we are testing for the possibility that 1 or more genes may confer susceptibility to myeloid leukemia in the rabbit. Also, crosses between respective transmitters of susceptibility to myeloid leukemia and lymphosarcoma (Is/+) should help us decide on the question of allelism. Our studies and those of others have clearly demonstrated that the development and frequency of rabbit tumors are greatly influenced by age, breed, and other constitutional factors.

We do not as yet know whether rabbit lymphosarcoma of WH rabbits is a virus-caused disease requiring a genetic predisposition. Our pedigree data on lymphosarcoma are consistent with concepts of both genetic susceptibility and vertical transmission of a viral genome. Our attempts at virus demonstration and, hopefully, isolation will now be extended to include strains III and III ep. Identification of a type C viral genome in rabbits would add another species to those in which its presence is known.

REFERENCES

Fig. 1.  

a, lymphoid atrophy and fibrotic red pulp, spleen. H & E, X 150; 
b, leukemic myeloid cells within trabecular spaces and vessels of lymph node. H & E, X 425; 
c, leukemic infiltration into liver lobule and around periportal triad by myeloid cells. There is some fibrosis and the blood vessel contains large numbers of tumor cells. Giemsa, X 150; 
d, details of cell types and leukemic liver infiltrations. The vein is packed with tumor cells, many of which are young neutrophils. H & E, X 350.
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